ORIGINAL ARTICLE

Predictors of Cardiovascular Disease Using Framingham Risk Score in a Rural Population

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ABSTRACT

Introduction: Identification of risk factors for cardiovascular disease (CVD) will apprise preventive measures in at-risk individuals. As CVD is becoming more prevalent among the rural communities in Malaysia, identifying predictors for high risk of CVD as a part of primary prevention is urgently required. The aim of this study was to determine the determinants of future CVD using FRS. **Methods:** This community-based study involved adults in several rural communities in the district of Raub, Malaysia between 2010 to 2011. Demographic data, anthropometric measurement and fasting blood assays were obtained. The risk of future cardiovascular event was determined using the "Framingham Heart Study" online calculator. **Results:** Among the 436 rural subjects, 58.3% were females. The mean age was 58.4 years (SD±10). According to FRS, 42.4% of the respondents were at high-risk of developing CVD in the next 10 years. All cardiovascular risk factors were significantly associated with FRS ($p<0.001$), except for total cholesterol. In the multivariable linear regression analysis, predictors of high FRS were waist-hip ratio (WHR) (β =13.37; 95% CI (6.18-28.9)), hypertension (β =2.44; 95% CI (2.17-2.74)), smoking (β =2.38; 95% CI (2.01-2.81)), diabetes (β =1.82; 95% CI (1.59-2.08)) and high LDL cholesterol (β =1.23; 95% CI (1.11-1.38)). **Conclusion:** Almost half of the population in this study were at high-risk of future cardiovascular events. WHR, hypertension, smoking, diabetes and high LDL were the main predictors for high FRS.
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Keywords: Non-communicable disease, Risk factors, Framingham risk scores, Cardiovascular diseases, Rural

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INTRODUCTION

The major causes of morbidity and mortality in most industrialized and developing countries worldwide is cardiovascular disease (CVD) (1). In addition, there is a rising prevalence in the mortality rate of individuals with CVD in rapidly developing countries compared to developed countries (2, 3). Changes in lifestyle and diet, coupled with economic development, could be the reasons for this increase (4). Malaysia is one of the developing countries in Asia which is facing an emergence of cardiovascular morbidity and mortality (5).

A number of well-established risk factors are involved in the development of CVD, such as hypertension, hyperglycemia, obesity (6), smoking (7) and hypercholesterolemia (8). CVD usually occur as a consequence of these risk factors (9). Therefore, these cardiovascular risk factors can be utilized to estimate the risk of developing CVD. Findings from the National Health and Morbidity Survey (NHMS), 2011, revealed that at least 63% of Malaysian adults had at least one cardiovascular risk factor, such as high blood pressure, high blood sugar, being overweight/obese or high cholesterol (10). Additionally, findings from the NHMS, 2019 showed that 1.7 million people in Malaysia currently live with the three major cardiovascular risk factors (hypertension, diabetes and hyperlipidaemia), while 3.4 million people in Malaysia have two of the three major risk factors (11).

The prevalence of non-communicable diseases in Malaysia is on an increasing trend for the past two decades. The same trend was reported for cardiovascular risk factors. In response to the high prevalence of cardiovascular risk factors among Malaysians, the Ministry of Health has formulated a few strategies. The National Strategic Plan for Non-Communicable Diseases (NSP-NCD) 2010-2014 and the NCD Prevention 1 Malaysia programs were established. The programs promote risk factor screenings and intervention in the communities (12, 13).

Nonetheless, the assessment of a single cardiovascular risk factor is indeed inadequate to estimate the risk of developing CVD in the future. However, the use of appropriate measurement tools may provide better estimations. The Framingham Risk Scores (FRS) may serve as a useful tool in assessing the probability of developing cardiovascular events in the future. The FRS offer a pragmatic depiction about the patient's risk of developing CVD in the next 10 years. The tool assists in cardiovascular risk factor management and treatment strategies, especially as part of a primary prevention (14). Moreover, the tool may be extended to populations which are often overlooked.

The rural populations, for example, is not exempted from CVD although thought to be at low risk. This population is experiencing an epidemiologic transition as an effect of rapid industrialization and urbanization. As a result, the rural population now experiences an epidemic of CVD (15). Prevention and intervention is challenging, as some rural populations might face challenges and difficulties in accessing healthcare services (16), due to their locality and availability of healthcare facilities. Hence, dissemination of health information and delivery of healthcare services to the rural populations of Malaysia might have yet to reach their maximum capacity.

Assessment of CVD risk factors is important for preventive measures. In addition, estimation of individuals' risk of developing future cardiovascular events based on the absolute risk is vital to divert the onset of the disease. Absolute risk assessment may only not serve as a platform to help make decisions on treatment, but also for risk communication to the patients (17). The Framingham Heart Study has identified that CVD is multifactorial and incorporates non-modifiable and modifiable risk factors in its 10-year prediction model (18).

The main predictors of future cardiovascular events among the rural population of Malaysia remains unknown. Hence, this study was conducted to identify the determinants for future CVD using a 10-year risk estimate of FRS in a rural community of Malaysia.

MATERIALS AND METHODS

This cross-sectional, community-based study was conducted between July 2010 and June 2011 in a rural community in the district of Raub, in Pahang, a state of West Malaysia. The detailed methodology of this study is described elsewhere (19). Briefly, the population in this study was selected by random sampling. Each household in this population was assigned a number which were then randomly selected to participate in this study. Within the rural community, 1459 households were assigned and 500 households were selected. Adults from the household aged above 30 years were invited to participate in this study. Participants with no history of coronary heart disease, stroke, peripheral vascular disease and were not on medication for hypercholesterolemia were included in this study (20).

In total, 610 participants were recruited for this study. Investigators interviewed these participants for their socio-demographic, clinical characteristics and medication status. Inclusion criteria were community dwellers aged 30 years or above and provided an informed consent. A total of 174 participants were excluded due to their refusal to provide blood samples and missing data on their clinical cardiovascular risk factors. Thus, a total of 436 participants were included in the analysis. The study was conducted in local community halls and government clinics. Institutional ethics board approval was obtained prior to the commencement of the study [REC/UITM/2007(10)].

Cardiovascular risk factors assessment

Systolic and diastolic blood pressures were taken after the respondents had rested for about five minutes with their arms supported at the same level as the heart. Measurement of blood pressure was taken twice on the right arm, in a seated position by a physician or trained nurse, using a validated Omron Automatic Blood Pressure Monitor (Tokyo, Japan). The average of the two readings was recorded. Hypertension was diagnosed if blood pressure (BP) recording was 140/90 mmHg and above or respondents who were on anti-hypertensive medications. Waist-hip-ratio (WHR) was computed by dividing the waist circumference by the hip's circumference. Waist circumference was recorded at the end of normal expiration at the midway between the lowest rib margin and the iliac crest. Hip circumference was measured at the maximal circumference over the buttocks, at the widest level over the greater trochanters. Both circumferences were measured using a non-elastic fibreglass measuring tape, to the nearest 0.5 cm.

Respondents fasted overnight prior to blood collection and other measurements. Venous blood samples were obtained for fasting blood glucose and fasting serum lipid. Blood samples were centrifuged (Hettich Zentrifugen Rotofix 32, Germany) at 4000 r/min for seven minutes within two hours of collection. Fasting blood glucose level were estimated using the hexokinase enzymatic reference method by an automated analyser (Cobas Integra; Roche Diagnostics, Basel, Switzerland). Respondents with a fasting blood glucose level of 7.0 mmol/L and above, was currently on medications and with a known history of diabetes were classified as having diabetes mellitus (21). Lipid profiles (HDL-c, triglycerides and total cholesterol) were measured using enzymatic reference methods on an automated analyser (Cobas Integra; Roche Diagnostics, Basel, Switzerland). LDL-c levels were calculated using the Friedewald equation (22). The fasting serum lipid cut-off used in this study was TC≥5.2 mmol/L, LDL≥3.4 mmol/L, HDL ≤1.00 mmol/L and TG≥1.7mmol/L (23).

CVD risk was calculated using the lipid profile-based Framingham Heart Study online calculator. Respondents were categorized into three groups based on their risk scores, which were high-risk (>20%), moderate-risk (10 to 20%) and low-risk (< 10%). We chose the lipid profile-based Framingham Heart Study online calculator, since BMI-based calculation had previously overestimated the 10-year risk for CVD (24). Furthermore, the lipid profile-based calculator requires the measurement of HDL-c and cholesterol levels, whereas the BMI-based calculation requires lesser clinical-associated measurements (25).

Statistical analysis

SPSS version 20 was used to analyse the data. Mean and standard deviation (SD) were used for normally distributed continuous variables. Frequency and percentages were used for categorical variables. Chi-square test was used to determine the association between categorical data. A one-way analysis of variance (ANOVA) was employed to determine the association between FRS and cardiovascular risk factors. Predictors for developing CVD were determined using Multivariable Linear Regression. Prior to the regression analysis, all assumptions were ensured to have met the multivariable linear regression analysis. The linearity between FRS and cardiovascular risk factors, normality of residuals, homoscedasticity and multi-collinearity were checked. β-coefficient and 95% confidence interval (95% CI) were reported for the significant predictors of FRS.

RESULT

Table I depicts the prevalence of cardiovascular risk factor profile among the rural respondents. The mean age of the respondents was 58.4 years (SD±10) whereby females accounted for 58.3% of the participants. Majority of the respondents had completed primary school education (66%) and were married (85.7%). The prevalence of current smokers was 11.7%, with majority of the smokers being males and representing 27.5% (p<0.001) of the participants. About 61.2% of the respondents had hypertension but only 29.4% of them were taking their prescribed medication. The prevalence of diabetes mellitus was 22.9%, with males having significantly higher prevalence compared to females. Almost two-thirds of the participants (64.2%) had high total cholesterol levels. About a third of the respondents had low HDL-cholesterol (38.5%) and high LDL-cholesterol (38.3%). Meanwhile, nearly half of the participants (48.4%) had high levels of triglycerides. The proportion of high-risk respondents for CVD via lipid profile-based method was 42.4%. Males made up a significantly higher percentage of the high-risk group, compared to females (63.2% vs 27.6%).

Table I: Cardiovascular risk factor profile among the rural respondents (n=436)

	Prevalence (%)			
Cardiovascular Risk Factors	**All (n=436)**	**Males (n=182)**	**Females (n=254)**	**p-value**
Age, years	58.4±10	60.2±9.6	57.2±10.1	p<0.05
Current smokers	11.7	27.5	0.4	p<0.001
Hypertension	61.2	59.9	62.2	0.12
Diabetes	22.9	26.4	20.3	p<0.05
Total cholesterol (≥5.2mmol/L)	64.2	59.3	67.7	0.09
Low HDL-c (≤1.00mmol/L)	38.5	52.7	28.3	p<0.001
High LDL-c (≥3.4mmol/L)	38.3	35.2	40.6	0.23
Triglycerides (≥1.7mmol/L)	48.4	57.1	42.1	p<0.05
Framingham Risk Score				
Low Risk (FRS<10%)	29.4	8.2	44.5	
Moderate Risk (FRS 10-20%)	28.2	28.6	28.0	p<0.001
High Risk (FRS>20%)	42.4	63.2	27.6	

*FRS: Framingham Risk Score; HDL: high density lipoprotein; LDL: low density lipoprotein.

Table II illustrates the association between cardiovascular risk factors and FRS groups. As expected, the older respondents had a higher CVD risk as compared to the younger respondents (p<0.001). The high-risk group had significantly higher systolic blood pressures (SBP) and diastolic blood pressures (DBP) with 88.6% being hypertensive and 39.5% having diabetes mellitus (p<0.001). Fasting blood glucose, LDL-c levels, triglycerides, and prevalence of smokers were significantly higher in the high-risk group (p<0.05).

Meanwhile, the HDL-c level was significantly lower in the high-risk group (p<0.001).

Table II: Cardiovascular risk factors and their association with FRS

Cardiovascular Risk Factors	Mean±SD/n (%)			p-value
	Low Risk (FRS<10%)	Moderate Risk (FRS 10-20%)	High Risk (FRS>20%)	
Age, years	51.2±7.3	57.3±8.6	64.2±9	p<0.001
SBP, mmHg	124±13	138±14.6	156±21	p<0.001
DBP, mmHg	79±9.8	83±11	88±12.7	p<0.001
Fasting blood glucose, mmol/L	5.4±1.6	5.8±2.2	6.9±3.2	p<0.001
Total cholesterol, mmol/L	5.4±1	5.5±1.1	5.7±1.2	0.130
HDL-c, mmol/L	1.3±0.31	1.2±0.31	1.1±0.28	p<0.001
LDL-c, mmol/L	3.4±0.92	3.5±0.94	3.7±1.08	p<0.05
Tri-glycerides, mmol/L	1.5±0.75	1.6±0.61	2.1±0.87	p<0.001
Current smokers, n (%)	1(0.8)	12(9.8)	38(20.5)	p<0.001
Medication adherence, n (%)	17(13.5)	27(22.5)	82(44.3)	p<0.001
Hypertension, n (%)	34(26.6)	69(56.1)	164(88.6)	p<0.001
Diabetes, n (%)	9(7.1)	17(13.9)	73(39.5)	p<0.001

*BP: blood pressure; FRS: Framingham Risk Score; HDL: high density lipoprotein; LDL: low density lipoprotein; SD: standard deviation. Values are presented as n(%) unless otherwise indicated.

Table III shows the multivariable linear regression analysis, with FRS being the dependant variable. It further denotes that the predictors for developing CVD were elevated for participants with a specific WHR (β = 13.37, [95% CI: 6.18 to 28.9]), hypertension (β = 2.44, [95% CI: 2.17 to 2.74]), smoking (β = 2.38, [95% CI: 2.01 to 2.81]), diabetes mellitus (β = 1.82, [95% CI: 1.59 to 2.08]) and high LDL concentration (1.23, [95% CI: 1.11 to 1.38]).

DISCUSSION

In the present study, factors associated with future cardiovascular events were predicted by the lipid profile-based Framingham Heart Study online calculator. Elevated WHR, high LDL-c levels, smoking and suffering from hypertension, and diabetes mellitus were significant predictors for future cardiovascular events.

It was revealed that WHR was the main predictor of high FRS. Respondents with elevated WHR are at higher risk of developing CVD in the future. A meta-regression analysis of prospective studies in Canada discovered that the risk of CVD incident increases with increasing WHR or waist circumference (26). This anthropometric measure of abdominal obesity has been proposed to be a superior predictor for developing CVD. This is because the measurement includes hip circumference, which is inversely associated with other cardiovascular risk factors such as dyslipidaemia, hypertension, and diabetes mellitus (26). A similar result was found in a study conducted among Spanish Caucasian adults, in which it was concluded that WHR is the best predictor according to the Systematic Coronary Risk Evaluation (SCORE) chart (27). Moreover, a meta-analysis study revealed that WHR is a strong predictor of myocardial infarction, particularly among women (28).

Table III: CVD predictors associated with Framingham Risk Score among the study population (n=436)

Variables	SLR[a]			MLR[b]			
	Unadjusted β [c]	(95% CI)	p-value	Adjusted β [d]	(95% CI)	t-stat	p-value
Hypertension	2.81	(2.44, 3.23)	<0.001	2.44	(2.17, 2.74)	15.27	<0.001
Diabetes	2.25	(1.88, 2.70)	<0.001	1.82	(1.59, 2.08)	8.83	<0.001
High LDL-c	1.14	(0.97, 1.35)	0.114	1.23	(1.11, 1.38)	3.76	<0.001
Smoker	2.28	(1.79, 2.92)	<0.001	2.38	(2.01, 2.81)	10.08	<0.001
WHR	1.23	(1.02, 1.50)	0.034	13.37	(6.18, 28.90)	6.60	<0.001

[a] Simple Linear Regression
[b] Multivariable Linear Regression (R2=59.1%; The model fits reasonably well; Model assumption are met; no multicollinearity problem)
[c] Crude regression coefficient
[d] Adjusted regression coefficient
*LDL: low density lipoprotein; WHR: waist hip ratio

According to the FRS, the majority of respondents in the high-risk group, which accounted for 88% of the total population in this rural community, had significant hypertension with higher mean SBP and DBP values compared to other FRS groups. There is sufficient evidence to demonstrate that hypertension drives CVD. According to a study conducted among urban minority adults in New York, researchers found that hypertension is the main driver for the development of CVD (29). Additionally, the Asia Pacific Cohort Studies Collaboration (APCSC) also demonstrated that hypertension had a high population-attributable fraction for CVD in the Asian countries (30). Due to its high prevalence and subsequent cardiovascular complications, hypertension continues to be a significant global health challenge.

Numerous national reports have documented that the prevalence of hypertension is increasing in low- and middle-income countries, while it is decreasing or remaining stable in high-income countries (31-34). In Malaysia, control of hypertension has been improved over the years, but the success rates remain low (35). Additionally, the prevalence of hypertension in rural areas were alarming. The prevalence of hypertension was reported at 41.3% among indigenous communities in Sabah (36), 29.8% in the rural areas of Penang (37) and 33.6% among adults in rural Kedah (38). Meanwhile, data from the National Health and Morbidity Survey (2015) and REDISCOVER Study showed that the prevalence of hypertension among adults in the rural population was 33.5% and 51.2%, respectively (10, 35).

Smoking status was also a significant predictor for future cardiovascular events. Cigarette smoking has been confirmed as one of the risk factors for stroke in both men and women (39). Tobacco exposure significantly increases the risk of coronary plaque rupture, which promotes the formation of thrombus and subsequently leading to the sudden onset of acute coronary syndrome (40, 41). On average, individuals who smoke, lose 10 years of life compared to those who never smoked. Furthermore, smoking was found to be the main predictor of adult death from NCD (42).

Findings from our study suggest that any efforts to reduce the prevalence of smokers, such as smoking cessation programs or quit-smoking clinics, should be enhanced, since smoking cessation reduces the risk of morbidity and mortality. Those who have quit smoking have a significantly lower risk of developing CVD within 5 years of quitting (43). On a similar note, the risk of stroke is almost similar among smokers and non-smokers after 5 to 15 years of quitting (44).

It was also found that diabetes is one of the significant predictors for future cardiovascular events. This finding is not surprising, as national data had shown that the prevalence of diabetes had increased since 1996 (45). The association between diabetes and CVD is rather complex as it involves a combination of both genetic and metabolic factors. However, the risk factors for diabetes have been well established. Death due to CVD account for 44% in type 1 diabetes and 52% in type 2 diabetes (46). In the National Health and Nutrition Examination Survey study, 26.3% of stroke cases were also due to diabetes. Specifically, those who have diabetes will have a 2-fold greater risk for ischemic stroke and 50% higher probability of hemorrhagic stroke (47).

High LDL-c levels was also found to be one of the significant predictors for future cardiovascular events. Evidence have shown that elevated LDL-c heightens the risk of atherosclerosis and myocardial infarction (48). The National Cholesterol Education Program Adult Treatment Panel III also emphasized the importance of LDL-c as a main target for coronary heart disease risk reduction (49). Practicing a healthy lifestyle consisting of a well-balanced diet and regular physical activities are important preventive measures.

Additionally, our study discovered that males have a significantly higher risk of future cardiovascular events (63.2%) than females (27.6%). This is unsurprising given the high prevalence of cardiovascular risk factors among males in this study, including advanced age, smoking, diabetes, low HDL-c and elevated triglycerides levels. Our findings are consistent with studies with a larger sample size of Malaysians (24). Furthermore, a study of diabetic European patients found similar results, with females having a lower risk for a 10-year CVD risk assessment (50).

Moreover, our study revealed that all cardiovascular risk factors, excluding total cholesterol were significantly associated with the FRS. An increase in the level of each cardiovascular risk factor would increase the risk of developing CVD. Data from this study suggests that lifestyle modification programs should be delivered to the high-risk individuals in the community. These programs would improve the risk profiles and prevent the development of CVD in the community, including rural residents. These efforts could significantly curb the CVD epidemic.

Identifying factors of future cardiovascular events is important to drive preventive measures. These factors should be targeted for intervention and information about these risk factors should be delivered to the communities in the rural population. Subsequently, individuals with a higher risk of developing future cardiovascular events should change their behaviour and lifestyle to avert the onset of CVD.

Our study has some limitations. Firstly, due to the cross-sectional nature of this study, we could only ascertain the association between cardiovascular risk factor with a 10-year risk of future cardiovascular events. Causality between the variables studied and the hazard ratio for each risk factors are unknown. Hence, a prospective study is recommended in the future. Secondly, this study did not assess additional cardiovascular risk factors such as physical inactivity, diet, alcohol consumption or socio-economic status. However, our study incorporated important risk factors that were included in the lipid profile-based Framingham Heart Study online calculator and involved large number of participants. Finally, this study was conducted mainly among the Malay population within the rural community, suggesting that interpretation towards other ethnic groups should be cautiously made. Further studies are needed that incorporates more relevant and diverse risk factors to have a better understanding on CVD risk prediction.

CONCLUSION

It was discovered that nearly half of the rural population was at a high-risk of developing CVD, based on FRS. Significant predictors of future cardiovascular events included a high WHR, hypertension, smoking, diabetes mellitus and elevated LDL-c levels. It is critical to improve the status of these risk factors in order to minimize the risks of developing future cardiovascular events among the Malaysian rural population.

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